Jan Delaval please

Access DB# 67621

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabiha Qazi Examiner #: 74141 Date: 5/28/02

Art Unit: 1616 Phone Number 30 3 - 3910 Serial Number: 09/214,155

Mail Box and Bldg/Room Location: 2D19, CM1 3B07 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Vitamin D derivatives

Inventors (please provide full names): TAKAYAMA et al

Earliest Priority Filing Date: 5/2/1997

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search for compds of Cl. 3

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

****

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:	Jan	NA Sequence (#)		STN	✓
Searcher Phone #:	4498	AA Sequence (#)		Dialog	
Searcher Location:		Structure (#)	✓	Questel/Orbit	
Date Searcher Picked Up:	5/30/02	Bibliographic		Dr.Link	
Date Completed:	5/30/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:		Fulltext		Sequence Systems	
Clerical Prep Time:	15	Patent Family		WWW/Internet	
Online Time:	~40	Other		Other (specify)	

PTO-1590 (8-01)

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

=> fil reg
FILE 'REGISTRY' ENTERED AT 08:01:41 ON 30 MAY 2002

STRUCTURE FILE UPDATES: 28 MAY 2002 HIGHEST RN 422506-41-0
DICTIONARY FILE UPDATES: 28 MAY 2002 HIGHEST RN 422506-41-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

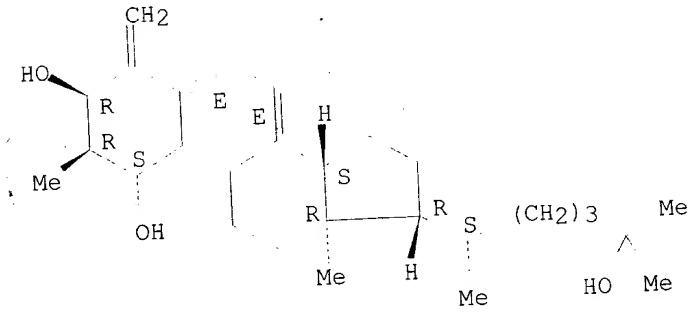
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d l30 ide can tot

L30 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 376591-49-0 REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5E,7E,20S)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

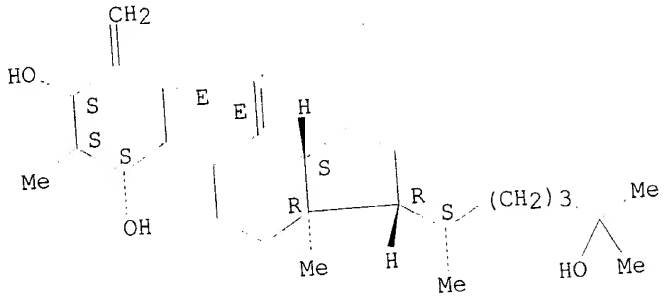
REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

L30 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 376591-48-9 REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5E,7E,20S)- (9CI)** (CA INDEX NAME)

FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

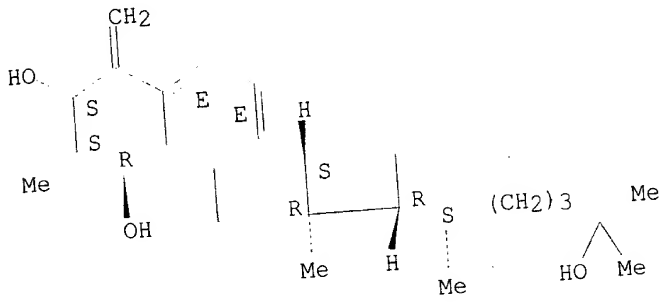
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

L30 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 376591-44-5 REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.beta.,5E,7E,20S)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

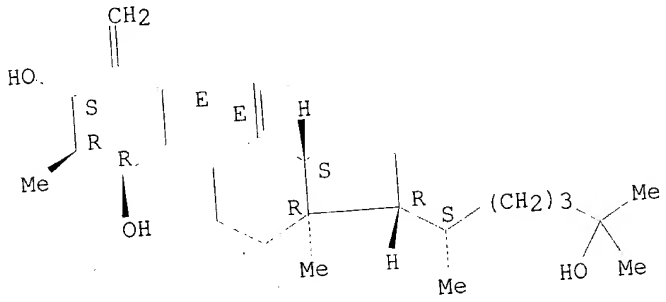
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

L30 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 376591-43-4 REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5E,7E,20S)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

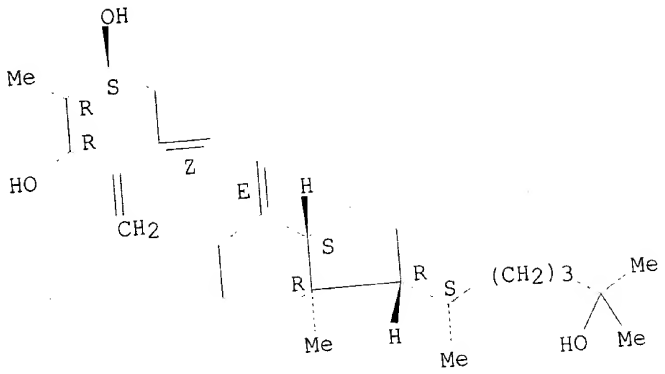
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

L30 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **214351-97-0** REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5Z,7E,20S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Cyclohexanediol, 2-methyl-4-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1S,2R,3R,5Z)-
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

REFERENCE 3: 134:353446

REFERENCE 4: 134:231493

REFERENCE 5: 134:29607

REFERENCE 6: 132:246451

REFERENCE 7: 129:343629

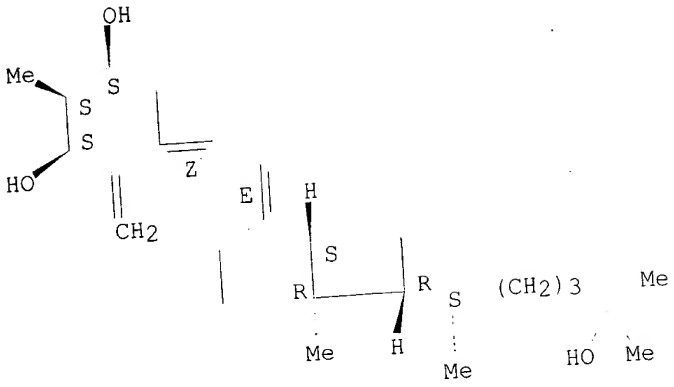
REFERENCE 8: 129:290279

L30 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **214351-94-7** REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5Z,7E,20S)- (9CI)** (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN 1,3-Cyclohexanediol, 2-methyl-4-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1S,2S,3S,5Z)-

FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

REFERENCE 3: 134:353446

REFERENCE 4: 134:231493

REFERENCE 5: 134:29607

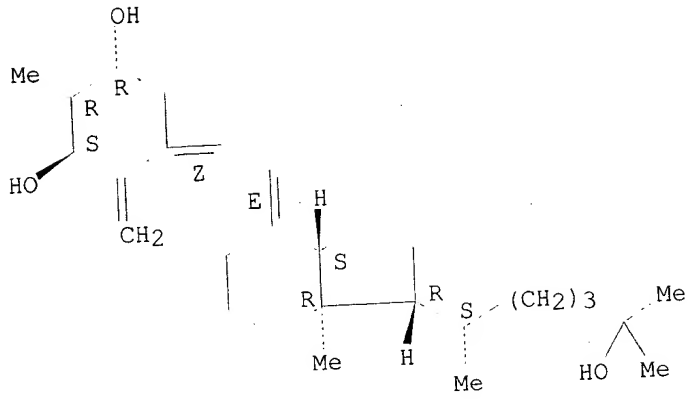
REFERENCE 6: 132:246451

REFERENCE 7: 129:343629

REFERENCE 8: 129:290279

L30 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN **214351-93-6** REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E,20S)- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methyl-4-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2R,3S,5Z)-
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

REFERENCE 3: 134:353446

REFERENCE 4: 134:231493

REFERENCE 5: 134:29607

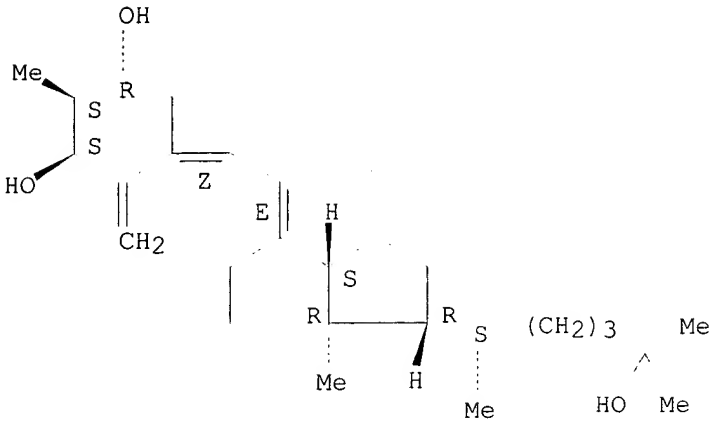
REFERENCE 6: 132:246451

REFERENCE 7: 129:343629

REFERENCE 8: 129:290279

L30 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 214351-84-5 REGISTRY
CN **9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.beta.,5Z,7E,20S)- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methyl-4-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2S,3S,5Z)-
FS STEREOSEARCH
MF **C28 H46 O3**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310070

REFERENCE 2: 136:6207

REFERENCE 3: 134:353446

REFERENCE 4: 134:231493

REFERENCE 5: 134:29607

REFERENCE 6: 132:246451

REFERENCE 7: 129:290279

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:01:51 ON 30 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 May 2002 VOL 136 ISS 22
FILE LAST UPDATED: 28 May 2002 (20020528/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please

check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all hitstr tot l38

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:745027 HCAPLUS
DN 129:343629
TI Preparation of **vitamin D3** derivatives and their pharmaceutical uses
IN **Takayama, Hiroaki; Konno, Katsuhiro; Fujishima, Toshie**
PA **Teijin** Ltd., Japan
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07C401-00
ICS A61K031-59
CC 32-7 (Steroids)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9850353	A1	19981112	WO 1998-JP1979	19980430	<--
	W: JP, US					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	EP 957088	A1	19991117	EP 1998-917742	19980430	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
PRAI	JP 1997-114695		19970502	<--		
	WO 1998-JP1979		19980430	<--		

OS CASREACT 129:343629; MARPAT 129:343629
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

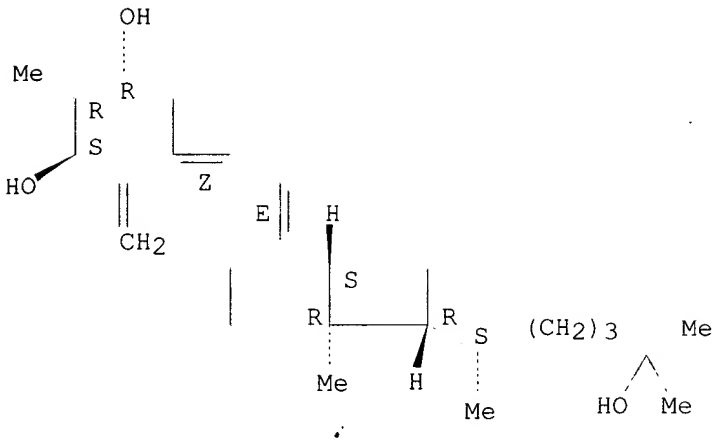
AB 1,25-Dihydroxy-2-Me **vitamin D3** derivs. I [R1, R2 = H, tri(C1-7alkyl)silyl; the asym. carbon atoms at the 1-, 2- and 3-positions each independently has an .alpha.- or .beta.-configuration], useful as remedies for osteoporosis, rachitis, accessory thyroidal hyperenergia, etc., are prepd. via reaction of II (X = bromo, iodo) with III (R3, R4 = H, trihydrocarbylsilyl) in the presence of a palladium catalyst optionally followed by deprotection (removal of silyl groups). Thus, II (X = Br) was reacted with III (R3 = R4 = TBS) in toluene contg. Et3N, Pd2(dba)3.CHCl3, and Ph3P at 120.degree. to give IV (R = TBS), which was treated with camphor-10-sulfonic acid in methanol to give 63% IV (R = H). In a study using 1.alpha.,25-**dihydroxyvitamin D3** receptors in the bovine thymus gland, this showed an affinity of 160 compared with 100 for 1.alpha.,25-**dihydroxyvitamin D3**.

ST **vitamin D3** deriv prepn biol use; osteoporosis therapy **vitamin D3** deriv prepn; rachitis therapy **vitamin D3** deriv prepn; thyroidal hyperenergia therapy **vitamin D3** deriv

IT Thyroid gland, disease
(hyperengergia; prepn. of **vitamin D3** derivs. and

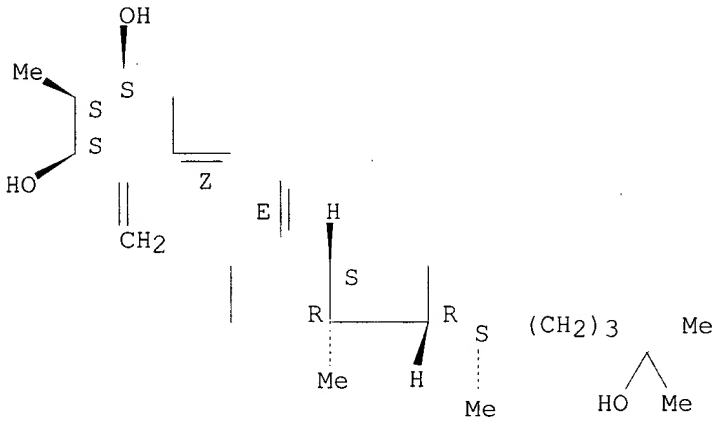
their pharmaceutical uses)
IT Rickets
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT Osteoporosis
(therapeutic agents; prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT 158388-11-5P **214351-93-6P 214351-94-7P** 214351-95-8P
214351-96-9P **214351-97-0P** 214351-98-1P 214351-99-2P
215394-65-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT 52522-40-4
RL: CAT (Catalyst use); USES (Uses)
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT 67-64-1, 2-Propanone, reactions 1066-54-2, Ethynyltrimethylsilane
18162-48-6, tert-Butyldimethylsilyl chloride 20445-33-4 39637-99-5
69739-34-0, tert-Butyldimethylsilyl triflate 143705-63-9 214351-89-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT 104701-87-3P 112057-64-4P 147915-53-5P 147915-54-6P 203126-90-3P
215394-09-5P 215394-10-8P 215394-12-0P 215394-15-3P 215394-17-5P
215394-20-0P 215394-22-2P 215394-23-3P 215394-24-4P 215394-25-5P
215394-26-6P 215394-27-7P 215394-28-8P 215394-29-9P 215394-30-2P
215394-31-3P 215394-32-4P 215394-33-5P 215394-34-6P 215394-35-7P
215394-36-8P 215394-37-9P 215394-38-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
IT **214351-93-6P 214351-94-7P 214351-97-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **vitamin D3** derivs. and their pharmaceutical uses)
RN 214351-93-6 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



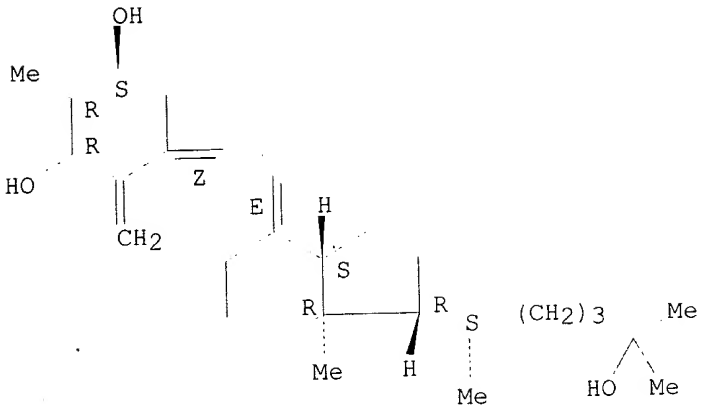
RN 214351-94-7 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 214351-97-0 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:606883 HCAPLUS
DN 129:290279
TI Synthesis and biological activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3
AU **Fujishima, Toshie**; Liu, Zhaopeng; Miura, Daishiro; Chokki, Manabu; Ishizuka, Seiichi; **Konno, Katsuhiro**; **Takayama, Hiroaki**
CS Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, 199-0195, Japan
SO Bioorganic & Medicinal Chemistry Letters (**1998**), 8(16), 2145-2148
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 32-7 (Steroids)
Section cross-reference(s): 1
AB Synthesis and biol. evaluation of all eight possible A-ring diastereomers of 2-methyl-20-epi-1,25-dihydroxyvitamin D3 are described. Among the analogs synthesized, 2.alpha.-methyl-20-epi-1.alpha.,25-dihydroxyvitamin D3 exhibited exceptionally high potency. The double modification of 2-Me substitution and 20-epimerization yielded analogs with unique activity profiles.
ST dihydroxyvitamin D3 analogs prepn; receptor binding cell differentiation calcium mobilization
IT Cell differentiation
(HL-60; synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitamin D binding; synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)
IT 32222-06-3P, 1.alpha.,25-Dihydroxyvitamin D3
RL: PNU (Preparation, unclassified); PREP (Preparation)
(Synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)
IT **214351-84-5P 214351-93-6P 214351-94-7P**
214351-95-8P 214351-96-9P **214351-97-0P** 214351-98-1P
214351-99-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

IT 104651-47-0 203126-90-3 214351-87-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

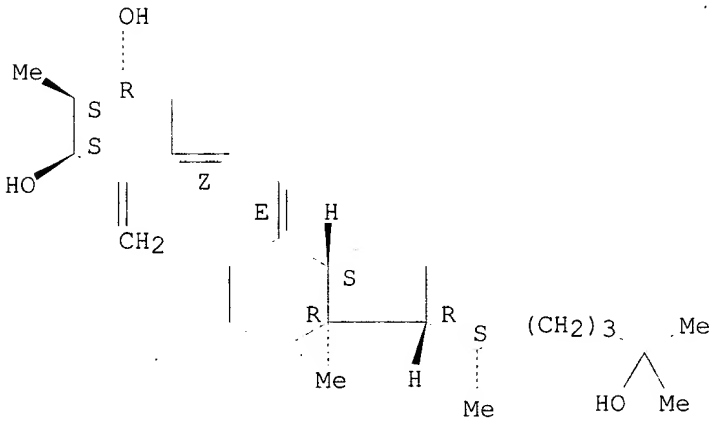
IT 171011-48-6P 183506-75-4P 213250-67-0P 214351-86-7P 214351-88-9P 214351-89-0P 214351-91-4P 214351-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport; synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

IT **214351-84-5P 214351-93-6P 214351-94-7P 214351-97-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

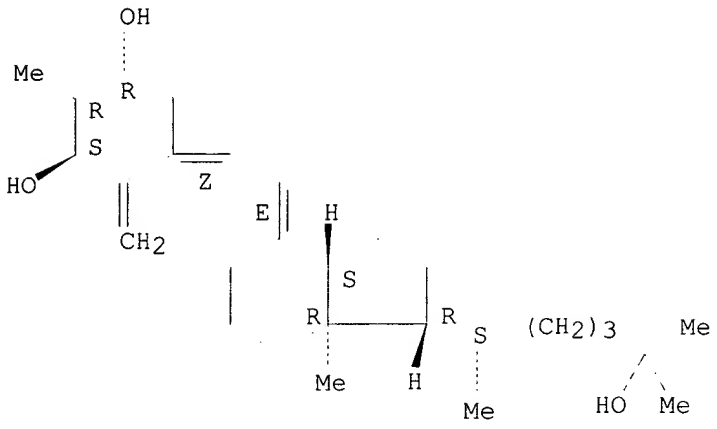
RN 214351-84-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



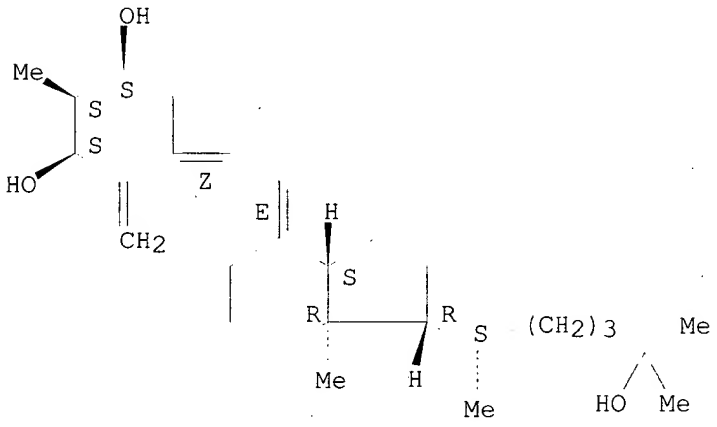
RN 214351-93-6 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



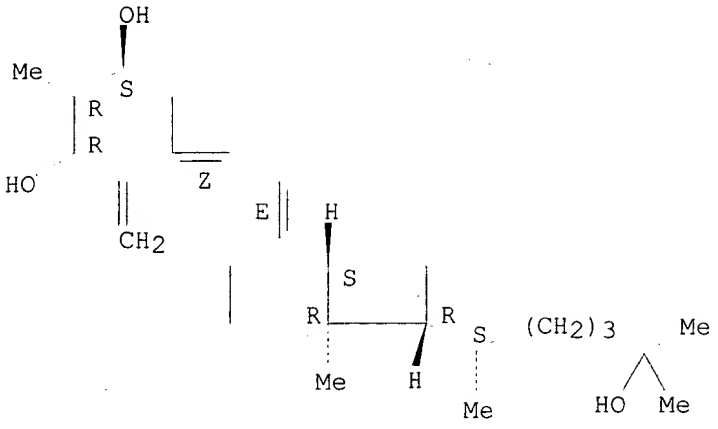
RN 214351-94-7 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 214351-97-0 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



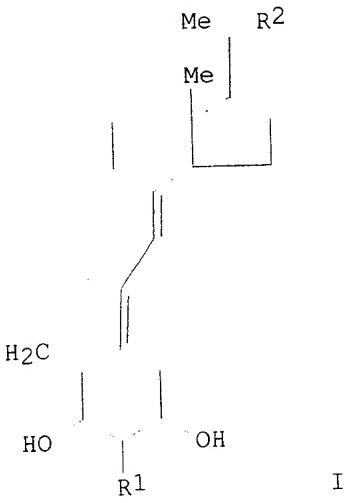
=> d bib abs hitrn tot

L42 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:868408 HCAPLUS
DN 136:6207
TI Preparation of 5,6-trans-2-alkylvitamin D derivatives
IN Takayama, Hiroaki; Fujishima, Toshie
PA Chugai Seiyaku Kabushiki Kaisha, Japan
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001090061	A1	20011129	WO 2001-JP4256	20010522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2000-151298 A 20000523
OS MARPAT 136:6207
GI



I

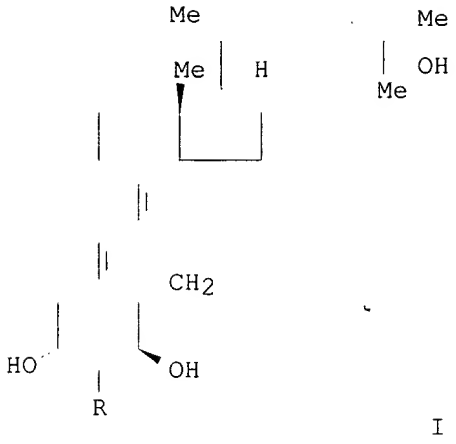
AB The title compds. I [R1 is linear or branched alkyl; and R2 is optionally hydroxylated linear or branched alkyl] are prepd. For example, (5E,7E)-(1S,2S,3R)-2-methyl-9,10-seco-5,7,10(19)-cholestatriene-1,3,25-triol was prepd. The affinity of compds. of this invention for the vitamin D receptor was demonstrated.

IT **376591-43-4P 376591-44-5P 376591-48-9P 376591-49-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 5,6-trans-2-alkylvitamin D derivs.)

IT **214351-84-5 214351-93-6 214351-94-7 214351-97-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 5,6-trans-2-alkylvitamin D derivs.)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:866554 HCAPLUS
DN 136:310070
TI Synthesis and biological evaluation of all A-ring stereoisomers of 5,6-trans-2-methyl-1,25-dihydroxyvitamin D3 and their 20-epimers: possible binding modes of potent A-ring analogues to vitamin D receptor
AU Fujishima, Toshie; Konno, Katsuhiro; Nakagawa, Kimie; Tanaka, Maki; Okano, Toshio; Kurihara, Masaaki; Miyata, Naoki; Takayama, Hiroaki
CS Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa, 199-0195, Japan
SO Chemistry & Biology (2001), 8(11), 1011-1024
CODEN: CBOLE2; ISSN: 1074-5521
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB The secosteroid 1.alpha.,25-dihydroxyvitamin D3 (I; R = H) has a wide variety of biol. activities, which makes it a promising therapeutic agent for the treatment of cancer, psoriasis and osteoporosis. Insight into the structure-activity relationships of the A-ring of I is still needed to assist the development of more potent and selective analogs as candidate chemotherapeutic agents, as well as to define the mol. mode of action. All possible A-ring stereoisomers of 5,6-trans-2-methyl-1,25-dihydroxyvitamin D3, e.g., I (R = .alpha.~ and .beta.-Me), and their 20-epimers were designed and efficiently synthesized. The dependence of the affinities for vitamin D receptor (VDR) and vitamin D binding protein (DBP), as well as the HL-60 cell differentiation-inducing activity, upon the stereochem. of the A-ring and at C20 in the side chain was evaluated. The binding affinities and potency of the 5,6-trans and 5,6-cis analogs were enhanced by a 2-Me substituent in a certain orientation. Mol. docking studies based upon the X-ray crystal structure of VDR suggested that the axial 2-Me group would be accommodated in a pocket surrounded by hydrophobic amino acid residues in the ligand binding domain, resulting in enhanced interaction.

IT **214351-84-5 214351-93-6 214351-94-7**
214351-97-0
RL: BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis and biol. evaluation of all A-ring stereoisomers of 5,6-trans-2-methyl-1,25-dihydroxyvitamin D3 and their 20-epimers)

IT **376591-43-4P 376591-44-5P 376591-48-9P**
376591-49-0P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of all A-ring stereoisomers of 5,6-trans-2-methyl-1,25-dihydroxyvitamin D3 and their 20-epimers)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:113244 HCAPLUS
DN 134:353446
TI Systematic studies on synthesis, structural elucidation, and biological evaluation of A-ring diastereomers of 2-methyl-1.alpha.,25-dihydroxyvitamin D3 and 20-epi-2-methyl-1.alpha.,25-dihydroxyvitamin D3
AU Takayama, H.; Konno, K.; Fujishima, T.; Maki, S.; Liu, Z.; Miura, D.; Chokki, M.; Ishizuka, S.; Smith, C.; DeLuca, H. F.; Nakagawa, K.; Kurobe, M.; Okano, T.
CS Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa,

199-0195, Japan
SO Steroids (2001), 66(3-5), 277-285
CODEN: STEDAM; ISSN: 0039-128X
PB Elsevier Science Inc.
DT Journal
LA English
AB All possible A-ring diastereomers of 2-methyl-1.alpha.,25-dihydroxyvitamin D3 and 20-epi-2-methyl-1.alpha.,25-dihydroxyvitamin D3 were synthesized by palladium-catalyzed coupling reaction of A-ring 'enyne' synthons with CD-ring portions. The A-ring synthons were rationally synthesized via a novel and practical route, starting with Me (R)-(+)- and (S)-(-)-3-hydroxy-2-methyl-propionate, in good yields. X-ray crystallog. anal. of 2.alpha.-methyl-1.alpha.,25-dihydroxyvitamin D3 (I) and conformational anal. of the A-ring of 2.alpha.-methyl- and 2.beta.-methyl-1.alpha.,25-dihydroxyvitamin D3 were carried out, and the results are described. All A-ring diastereomers, thus synthesized, were biol. evaluated both in vitro and in vivo. The biol. potency was highly dependent on the stereochem. of the A-ring substituents. In particular, I showed 4-fold higher vitamin D receptor [VDR] binding activity than the natural hormone, and its 20-epimer exhibited exceptionally high activity, 12-fold more potent in VDR binding, 7-fold in calcium mobilization, and 590-fold in induction of human promyelocytic leukemia (HL-60) cell differentiation as compared with the natural hormone. Further, the 20-epi-2.beta.-Me-1.beta.,3.alpha.(OH)2 isomer had significant biol. potencies compared to the natural hormone despite having 1.beta.-OH configuration. The transcriptional activities on human osteocalcin gene promoter, including VDRE in transfected mammalian cells, were also evaluated. Finally, there was a clear contrast between the effects of the 2-Me group on the HL-60 cell differentiation- and apoptosis-inducing activities.
IT **214351-84-5P 214351-93-6P 214351-94-7P**
214351-97-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, structural elucidation, and biol. evaluation of A-ring diastereomers of 2-methyl-1.alpha.,25-dihydroxyvitamin D3 and 20-epi-2-methyl-1.alpha.,25-dihydroxyvitamin D3)
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:854168 HCAPLUS
DN 134:231493
TI Structure-specific control of differentiation and apoptosis of human promyelocytic leukemia (HL-60) cells by A-ring diastereomers of 2-methyl-1.alpha.,25-dihydroxyvitamin D3 and its 20-epimer
AU Nakagawa, K.; Kurobe, M.; Konno, K.; Fujishima, T.; Takayama, H.; Okano, T.
CS Department of Hygienic Sciences, Kobe Pharmaceutical University, Kobe, 658-8558, Japan
SO Biochemical Pharmacology (2000), 60(12), 1937-1947
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
AB 1.alpha.,25-Dihydroxyvitamin D3 (1.alpha.,25(OH)2D3) has been shown to modulate not only proliferation and differentiation but also apoptosis of malignant cells, indicating that it would be useful for the treatment of hyperproliferative diseases such as cancer and psoriasis. Little information is available concerning structural motifs of the 1.alpha.,25(OH)2D3 mol. responsible for modulation of differentiation and apoptosis. The authors synthesized all possible A-ring diastereomers of

the 2-methyl-1.alpha.,25(OH)2D3 and its 20-epimer and evaluated their biol. activities in human promyelocytic leukemia (HL-60) cells. Surprisingly, the potent analogs could be clearly divided into two groups: (i) those bearing the 1.alpha.- and 3.beta.-hydroxyl groups on the A-ring were potent inducers of differentiation and growth inhibitors of HL-60 cells and (ii) those bearing the 1.beta.-hydroxyl group together with either 3.alpha.- or 3.beta.-hydroxyl groups on the A-ring were potent stimulators of apoptosis in these cells. The authors have clearly identified for the first time the structural motifs on the basis of the stereochem. of both hydroxyl groups at positions 1 and 3 of the A-ring of the 1.alpha.,25(OH)2D3 mol. responsible for the induction of differentiation and apoptosis of HL-60 cells. These findings provide useful information not only for structure-function studies of 1.alpha.,25(OH)2D3 analogs but also for the development of therapeutic agents for the treatment of leukemia and other cancers.

IT **214351-84-5 214351-93-6 214351-94-7**
214351-97-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-specific control of differentiation and apoptosis of human promyelocytic leukemia (HL-60) cells by A-ring diastereomers of methyldihydroxyvitamin D3 and its 20-epimer)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:692923 HCAPLUS
DN 134:29607
TI Synthesis, biological evaluation, and conformational analysis of A-ring diastereomers of 2-methyl-1,25-dihydroxyvitamin D3 and their 20-epimers: unique activity profiles depending on the stereochemistry of the A-ring and at C-20
AU Konno, Katsuhiro; Fujishima, Toshie; Maki, Shojiro; Liu, Zhaopeng; Miura, Daishiro; Chokki, Manabu; Ishizuka, Seiichi; Yamaguchi, Kentaro; Kan, Yukiko; Kurihara, Masaaki; Miyata, Naoki; Smith, Connie; DeLuca, Hector F.; Takayama, Hiroaki
CS Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko Kanagawa, 199-0195, Japan
SO Journal of Medicinal Chemistry (2000), 43(22), 4247-4265
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 134:29607
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB All eight possible A-ring diastereomers of 2-methyl-1,25-dihydroxyvitamin D3, e.g. I, and 2-methyl-20-epi-1,25-dihydroxyvitamin D3, e.g. II, were convergently synthesized. The A-ring enyne synthons III were synthesized starting with Me (S)-(+)- or (R)-(-)-3-hydroxy-2-methylpropionate. This was converted to the alc. IV as a 1:1 epimeric mixt. in several steps. After sepn. by column chromatog., each isomer led to the requisite A-ring enyne synthons III again as 1:1 mixts. at C-1. Coupling of the resulting A-ring enynes with the CD-ring portions in the presence of a Pd catalyst afforded the 2-Me analogs in good yield. In this way, all possible A-ring diastereomers were synthesized. The synthesized analogs were biol. evaluated both in vitro and in vivo. The potency was highly dependent on

the stereochem. of each isomer. In particular, the .alpha..alpha..beta.-isomer I exhibited 4-fold higher potency than 1.alpha.,25-dihydroxyvitamin D3 both in bovine thymus VDR binding and in elevation of rat serum calcium concn. and was twice as potent as the parent compd. in HL-60 cell differentiation. Furthermore, its 20-epimer, i.e., 20-epi-.alpha..alpha..beta. II, exhibited exceptionally high activities: 12-fold higher in VDR binding affinity, 7-fold higher in calcium mobilization, and 590-fold higher in HL-60 cell differentiation, as compared to 1.alpha.,25-dihydroxyvitamin D3. Accordingly, the double modification of 2-Me substitution and 20-epimerization resulted in unique activity profiles. Conformational anal. of the A-ring by 1H NMR and an X-ray crystallog. anal. of the .alpha..alpha..beta.-isomer I are also described.

IT **214351-84-5P 214351-93-6P 214351-94-7P**
214351-97-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation and conformational anal. of A-ring diastereomers of 2-methyl-1,25-dihydroxyvitamin D3 and 20-epimers and unique activity profiles depending on stereochem. of A-ring and at C-20)

RE.CNT 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:112653 HCAPLUS
DN 132:246451
TI Novel ring A stereoisomers of 2-Methyl-1.alpha.,25-dihydroxyvitamin D3 and 2-Methyl-20-epi-1.alpha.,25-dihydroxyvitamin D3: transactivation of target genes and modulation of differentiation in human promyelocytic leukemia (HL-60) cells
AU Nakagawa, K.; Kurobe, M.; Ozono, K.; Konno, K.; Fujishima, T.; Takayama, H.; Okano, T.
CS Department of Hygienic Sciences, Kobe Pharmaceutical University, Kobe, Japan
SO Biochemical Pharmacology (2000), 59(6), 691-702
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
AB The authors evaluated the biol. activity of two sets of ring A stereoisomers of 2-methyl-1.alpha.,25-dihydroxyvitamin D3 (2-methyl-1.alpha.,25(OH)2D3) and 2-methyl-20-epi-1.alpha.,25-dihydroxyvitamin D3 (2-methyl-20-epi-1.alpha.,25(OH)2D3) in terms of the following: transactivation of a rat 25-hydroxyvitamin D3-24-hydroxylase gene promoter including two vitamin D response elements (VDREs) and a human osteocalcin gene promoter including a VDRE in transfected human osteosarcoma (MG-63) cells; a vitamin D receptor (VDR)-mediated response using a VDR-GAL4 one-hybrid luciferase reporter system and a retinoid X receptor .alpha. (RXR.alpha.)-mediated response using an expressed VDR/RXR.alpha.-GAL4 modified two-hybrid luciferase reporter system in transfected human epithelioid carcinoma, cervix (HeLa) cells; and modulation of cell surface CD11b antigen expression in human leukemia (HL-60) cells. All the diastereomers of both analogs exhibited unique biol. activity profiles depending upon the configurations of the C-1 and C-3 hydroxyl groups, the C-2 Me group in ring A, and the C-20 Me group in the side chain. Of the eight possible diastereomers of the 2-Me analogs, 2.alpha.-methyl-1.alpha.,25(OH)2D3 was the most potent and exhibited comparable or even greater biol. potency than 1.alpha.,25(OH)2D3. Of the eight possible diastereomers of the 2-methyl-20-epi analogs, 2.alpha.-methyl-20-epi-1.alpha.,25(OH)2D3 was the most potent and exhibited 100- to 200-fold higher transcriptional potencies than 1.alpha.,25(OH)2D3 and exceptionally high cell regulatory activities.

2.beta.-Methyl-20-epi-1.alpha.,25(OH)2D3 was nearly as potent as its 2-epimer, 2.alpha.-methyl-20-epi-1.alpha.,25(OH)2D3, whereas its 20-epimer, 2.beta.-methyl-1.alpha.,25(OH)2D3, was almost completely biol. inactive. In these respects, it can be postulated that the double modification of 2-Me substitution and 20-epimerization to 1.alpha.,25(OH)2D3 induces remarkable changes in a VDR/RXR.alpha./VDRE-mediated signaling response and greatly enhances biol. activity. The other striking finding was that 2.beta.-methyl-20-epi-3-epi-1.beta.,25(OH)2D3 is transcriptionally more active than 1.alpha.,25(OH)2D3 despite lacking the 1.alpha.-hydroxyl group, which was believed to be essential for expressing VDR-mediated gene transcription. Since the C-20 natural counterpart, 2.beta.-methyl-3-epi-1.beta.,25(OH)2D3, was almost completely biol. inactive, 20-epimerization is probably responsible for activation of gene expression. Although earlier extensive structure-activity studies of vitamin D analogs showed stereochem. at the C-1, C-3, and C-20 of 1.alpha.,25(OH)2D3 to be the key structural motif for vitamin D action, the authors' results clearly demonstrated that stereochem. at the C-2 is also an important structural motif for vitamin D action and imply that 2-Me substitution possibly induces conformational changes in ring A depending upon the combinations of configurations of the C-1 and C-3 hydroxyl groups with C-20 stereochem. Consequently, several of these analogs exhibit exceptionally high or unexpected biol. activities at the mol. and cellular levels. These results suggest that 2-Me substitution together with alterations of stereochem. in both ring A and the side chain of 1.alpha.,25(OH)2D3 will provide useful analogs for structure-activity studies and development of therapeutic agents with unique biol. activity profiles.

IT **214351-84-5 214351-93-6 214351-94-7**
214351-97-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(transcriptional activity and cell regulatory effects of novel 2-methyl- or 2-methyl-20-epi-1.alpha.,25-dihydroxyvitamin D3 stereoisomers)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> fil reg
FILE 'REGISTRY' ENTERED AT 08:13:33 ON 30 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 28 MAY 2002 HIGHEST RN 422506-41-0
DICTIONARY FILE UPDATES: 28 MAY 2002 HIGHEST RN 422506-41-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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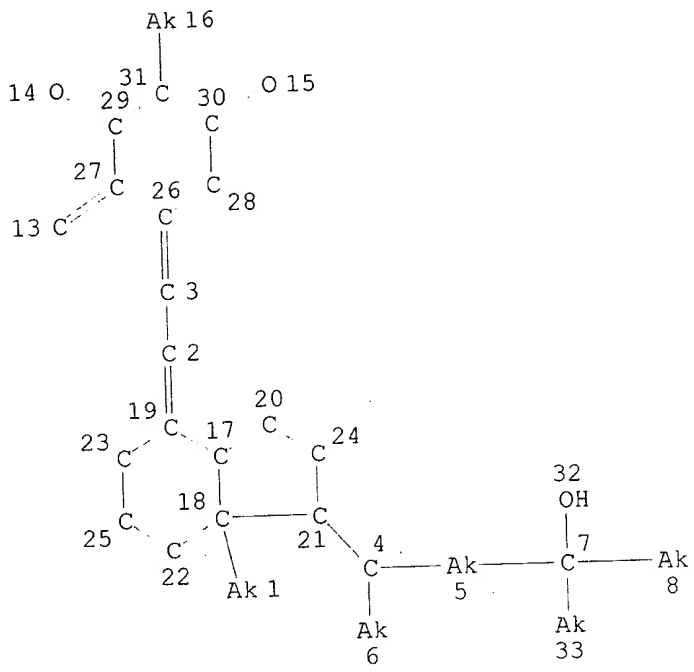
L45 STR



NODE ATTRIBUTES:
CONNECT IS M1 RC AT 14
CONNECT IS M1 RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L47 54 SEA FILE=REGISTRY CSS FUL L45

100.0% PROCESSED 5687 ITERATIONS 54 ANSWERS
SEARCH TIME: 00.00.01

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SAV TEMP L47 QAZI214155/A
L48 46 S L47 NOT L30

FILE 'HCAOLD' ENTERED AT 08:08:21 ON 30 MAY 2002
L49 0 S L48

FILE 'USPATFULL, USPAT2' ENTERED AT 08:08:27 ON 30 MAY 2002
L50 2 S L48

FILE 'HCAPLUS' ENTERED AT 08:09:05 ON 30 MAY 2002
L51 21 S L48
L52 8 S L51 AND (PD<=19980430 OR PRD<=19980430 OR AD<=19980430)
L53 4 S L52 AND L6
L54 8 S L52,L53

SEL HIT RN

FILE 'REGISTRY' ENTERED AT 08:10:12 ON 30 MAY 2002
L55 19 S E136-E154
L56 18 S L48 NOT 2 METHYL
L57 28 S L48 NOT L56

FILE 'HCAPLUS' ENTERED AT 08:12:35 ON 30 MAY 2002
L58 15 S L57
L59 6 S L58 AND (PD<=19980430 OR PRD<=19980430 OR AD<=19980430)
L60 12 S L58 AND L6
L61 4 S L59 AND L60
L62 6 S L59,L61

FILE 'USPATFULL, USPAT2' ENTERED AT 08:13:24 ON 30 MAY 2002
L63 2 S L57

FILE 'REGISTRY' ENTERED AT 08:13:33 ON 30 MAY 2002

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:13:46 ON 30 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 May 2002 VOL 136 ISS 22
FILE LAST UPDATED: 28 May 2002 (20020528/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l62 bib abs hitstr tot

L62 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:271054 HCAPLUS
DN 130:296894
TI Preparation of vitamin D3 derivatives for the treatment of osteoporosis
IN **Takayama, Hiroaki; Konno, Katsuhiro;** Maki, Shojiro
PA **Teijin** Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11116551	A2	19990427	JP 1998-160647	19970502 <--

PRAI JP 1996-235144 19960905 <--
JP 1996-314693 19961126 <--
JP 1997-114695 19970502 <--
OS MARPAT 130:296894
GI

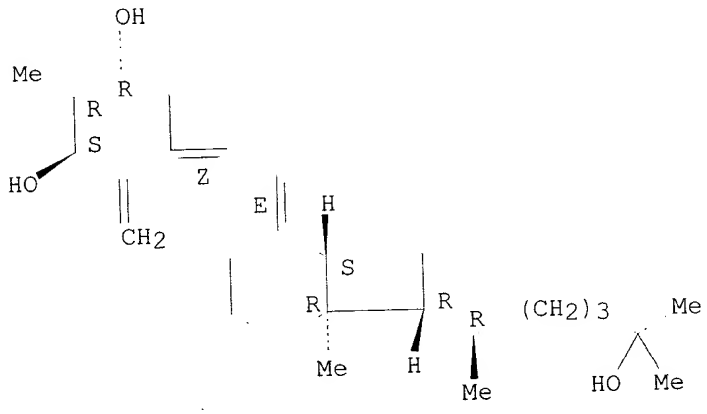
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 1,25-Dihydroxy-2-methylvitamin D3 derivs. of formula I [R1, R2 = H, alkyl] are prepd. for the treatment of osteoporosis. Thus, III was added to IV, then deprotected to give II. The vitamin D receptor affinity of II was 400, compared to 100 for 1.alpha.,25-dihydroxyvitamin D3.

IT **158388-11-5P 203126-73-2P 203126-91-4P**
203126-92-5P 203126-93-6P 203126-94-7P
203126-95-8P 203126-96-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of vitamin D3 derivs. for the treatment of osteoporosis)

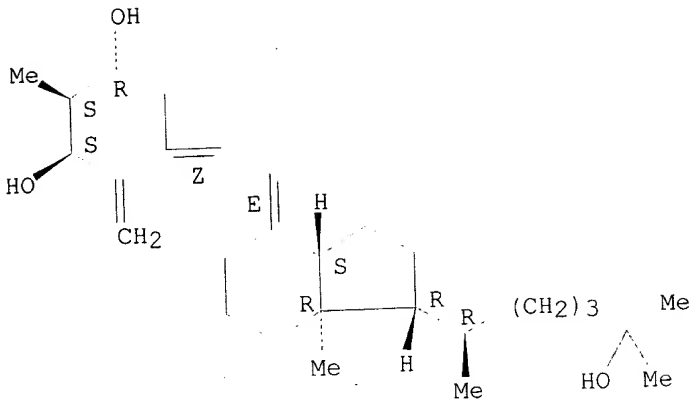
RN 158388-11-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



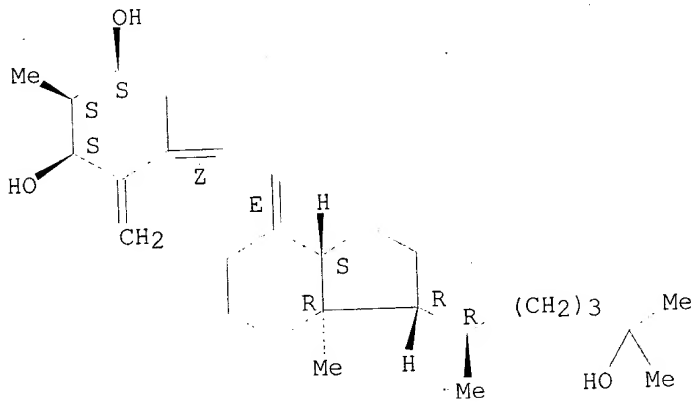
RN 203126-73-2 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



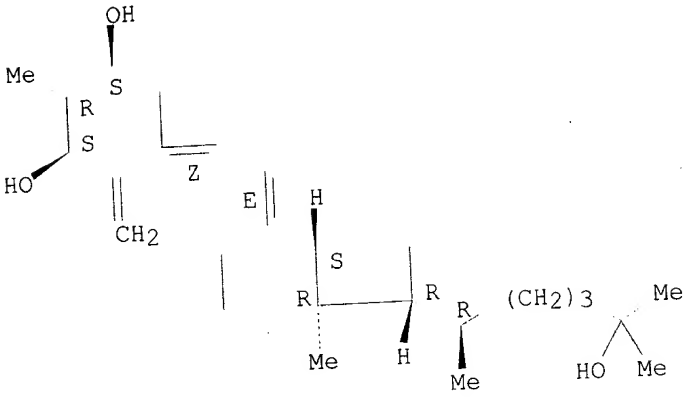
RN 203126-91-4 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



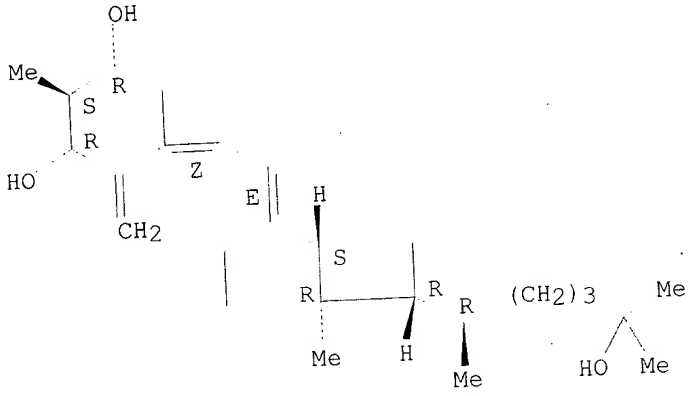
RN 203126-92-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



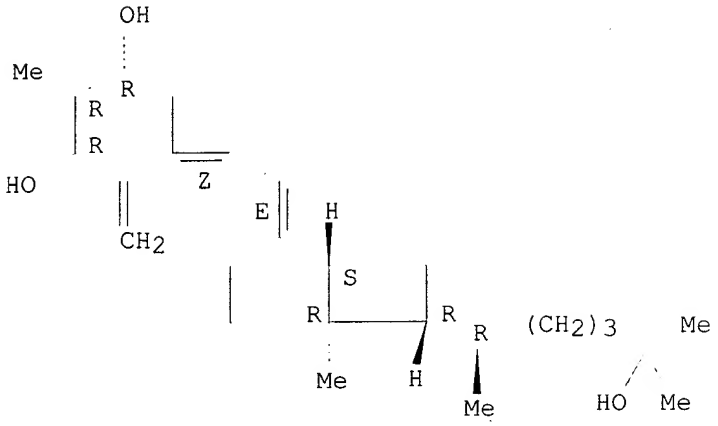
RN 203126-93-6 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



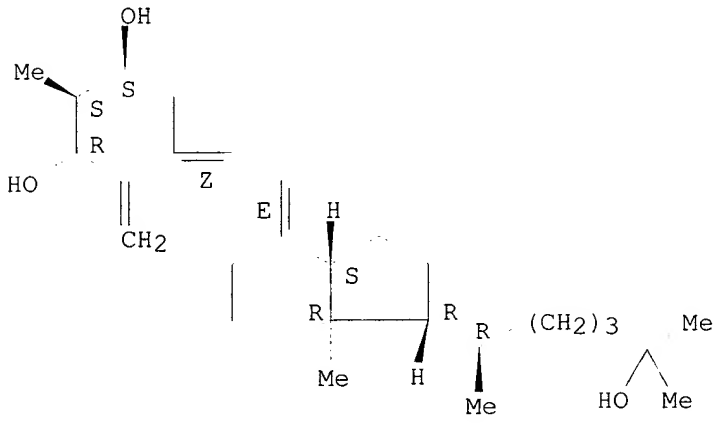
RN 203126-94-7 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



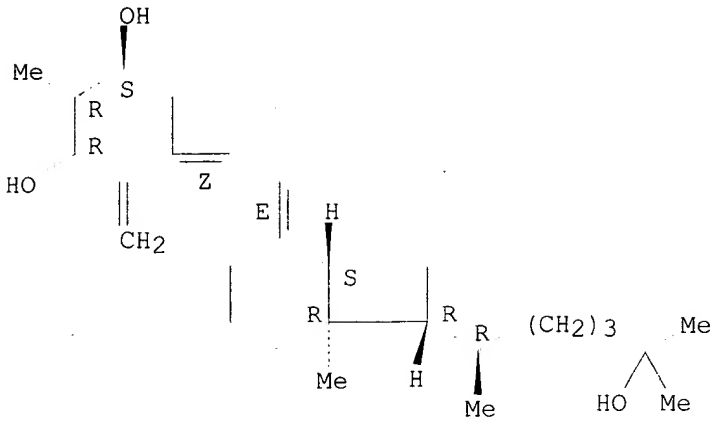
RN 203126-95-8 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



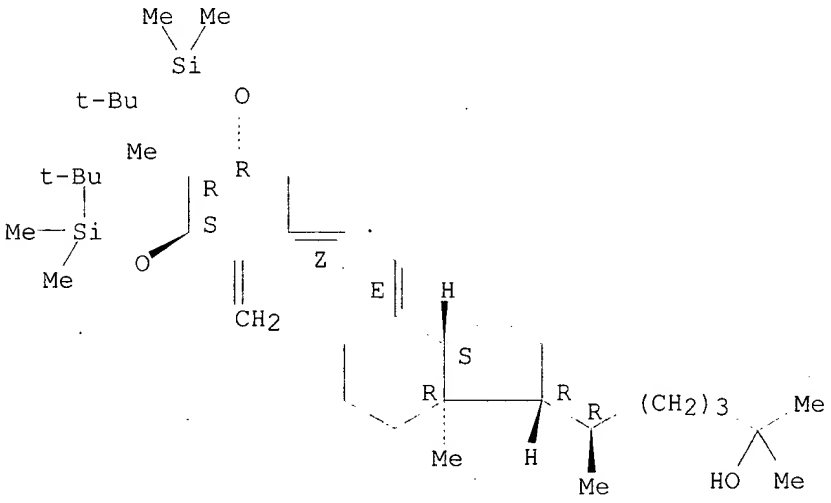
RN 203126-96-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **223437-60-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of vitamin D3 derivs. for the treatment of osteoporosis)
RN 223437-60-3 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

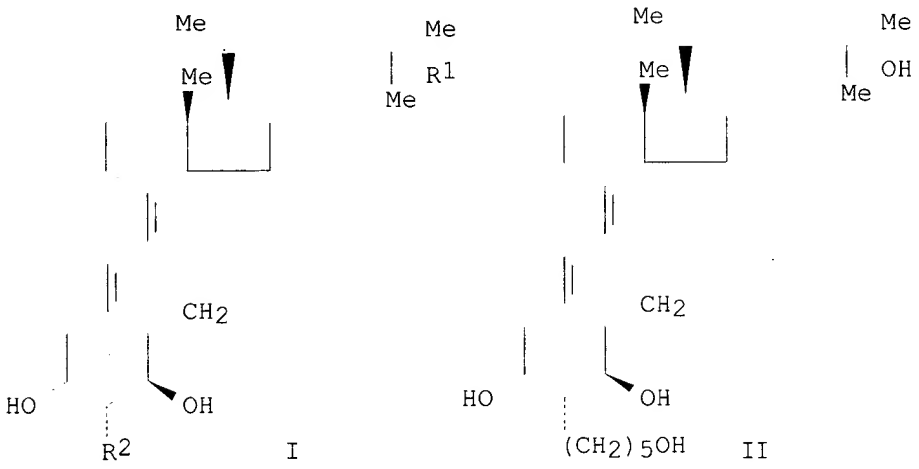
Absolute stereochemistry.
Double bond geometry as shown.



L62 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:155848 HCAPLUS
DN 130:209850
TI Preparation of vitamin D derivatives with substituent at the 2.beta.-position
IN Miyamoto, Katsuhito; Kubodera, Noboru
PA Chugai Seiyaku Kabushiki Kaisha, Japan
SO U.S., 17 pp., Cont. of U.S. Ser. No. 386,544, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 5877168	A	19990302		US 1996-706969	19960903	<--
	US 6124276	A	20000926		US 1998-116999	19980717	<--
PRAI	US 1995-386544	B1	19950210	<--			
	US 1996-706969	A3	19960903	<--			
OS	MARPAT 130:209850						

GI



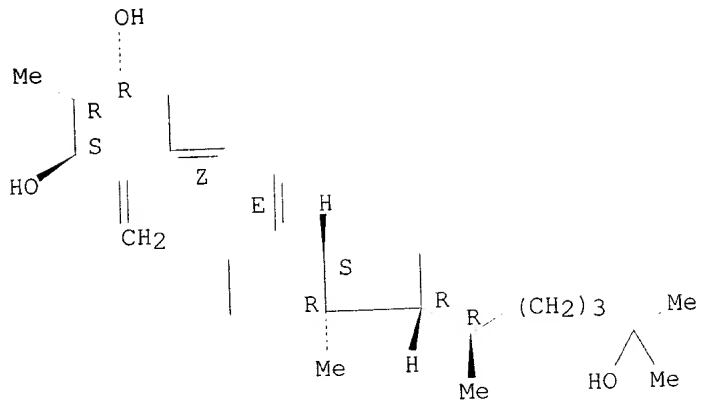
AB 1.alpha.-Hydroxy-vitamin D derivs. of formula I [R1 = H, OH; R2 = alkyl, alkenyl, alkynyl] are prepd. The compds. exhibit calcium metab. regulating activity and differentiation stimulating activity on tumor cells, etc. and are useful as a treating agent for diseases caused by abnormal calcium metab., such as osteoporosis and osteomalacia, or as an antitumor agent. Thus, II was prepd. from 5-bromo-1-pentene and 3.beta.,25-dihydroxy-1.alpha.,2.alpha.-epoxycholesta-5,7-diene, and showed bone formation activity.

IT **158388-11-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2.beta.-substituted vitamin D derivs. for the treatment of osteoporosis)

RN 158388-11-5 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:745027 HCAPLUS
DN 129:343629
TI Preparation of vitamin D3 derivatives and their pharmaceutical uses
IN **Takayama, Hiroaki; Konno, Katsuhiro; Fujishima, Toshie**
PA **Teijin** Ltd., Japan
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese

Inventors

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850353	A1	19981112	WO 1998-JP1979	19980430 <--
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 957088	A1	19991117	EP 1998-917742	19980430 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	JP 1997-114695		19970502 <--		
	WO 1998-JP1979		19980430 <--		

OS CASREACT 129:343629; MARPAT 129:343629
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

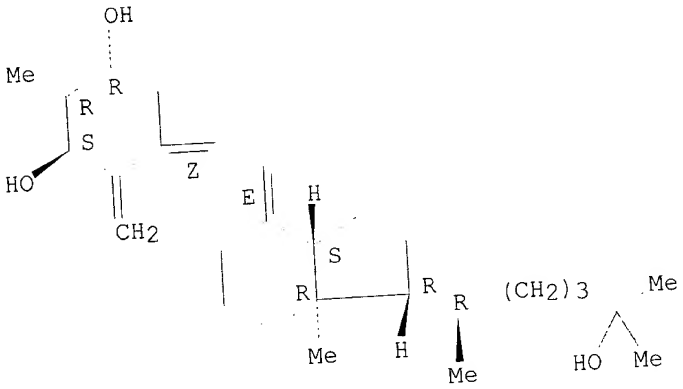
AB 1,25-Dihydroxy-2-Me vitamin D3 derivs. I [R1, R2 = H, tri(C1-7alkyl)silyl; the asym. carbon atoms at the 1-, 2- and 3-positions each independently has an .alpha.- or .beta.-configuration], useful as remedies for osteoporosis, rachitis, accessory thyroidal hyperenergia, etc., are prepd. via reaction of II (X = bromo, iodo) with III (R3, R4 = H, trihydrocarbylsilyl) in the presence of a palladium catalyst optionally followed by deprotection (removal of silyl groups). Thus, II (X = Br) was reacted with III (R3 = R4 = TBS) in toluene contg. Et3N, Pd2(dba)3.CHCl3, and Ph3P at 120.degree. to give IV (R = TBS), which was treated with camphor-10-sulfonic acid in methanol to give 63% IV (R = H). In a study using 1.alpha.,25-dihydroxyvitamin D3 receptors in the bovine thymus

gland, this showed an affinity of 160 compared with 100 for 1.alpha.,25-dihydroxyvitamin D3.

IT **158388-11-5P 214351-95-8P 214351-96-9P 214351-98-1P 214351-99-2P 215394-65-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of vitamin D3 derivs. and their pharmaceutical uses)

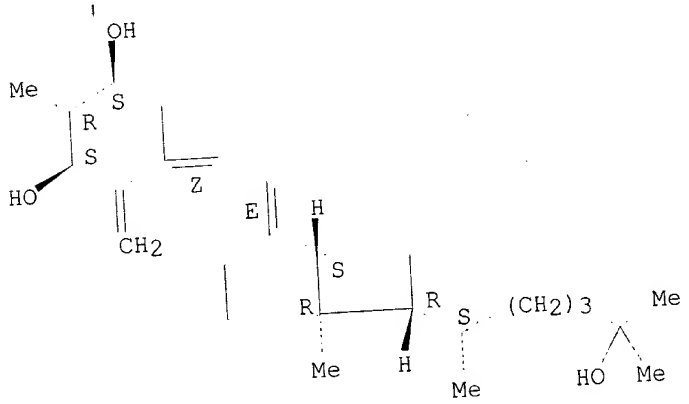
RN 158388-11-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



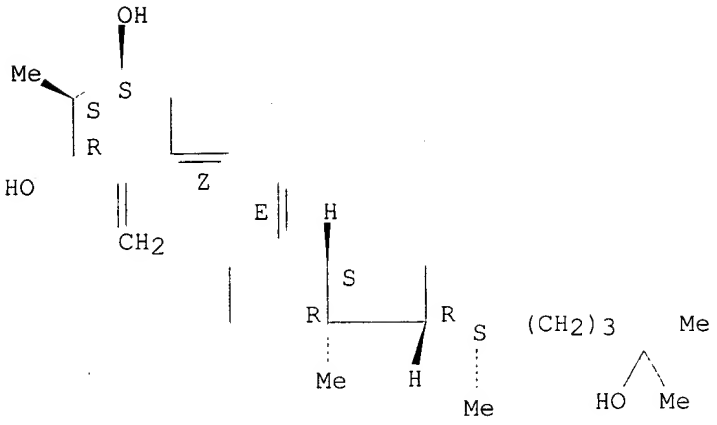
RN 214351-95-8 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



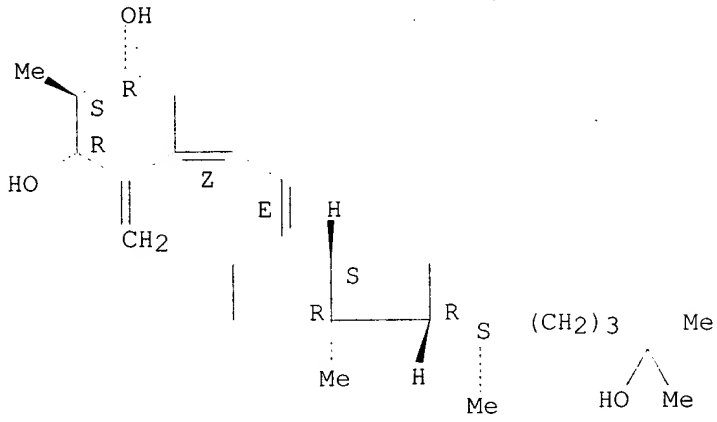
RN 214351-96-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



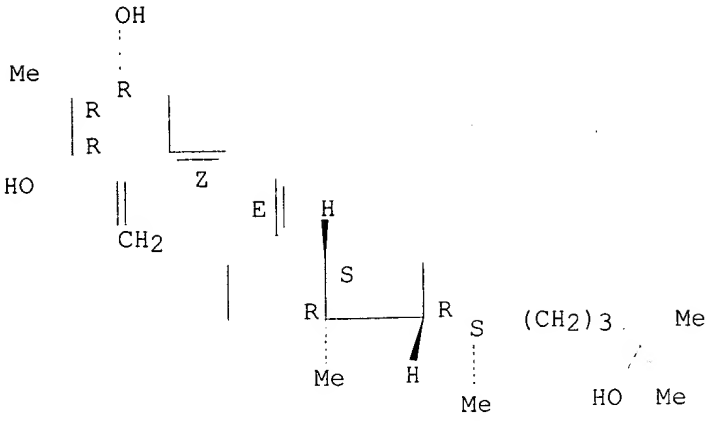
RN 214351-98-1 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



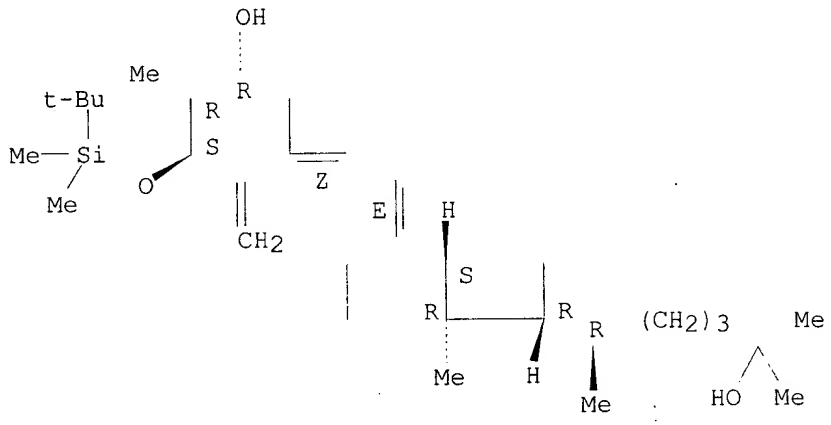
RN 214351-99-2 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 215394-65-3 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-triol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



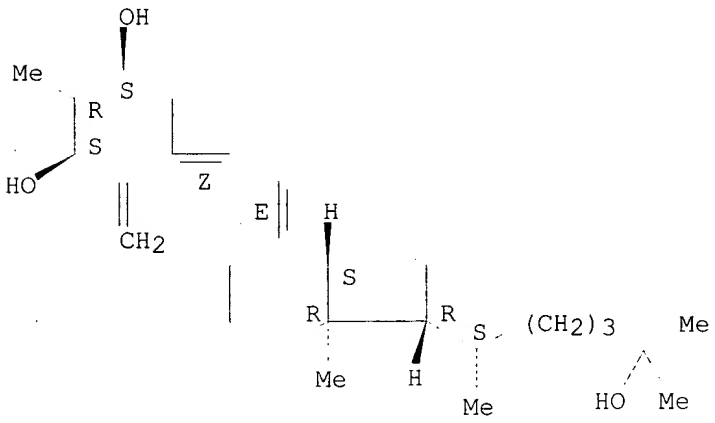
L62 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:606883 HCAPLUS
DN 129:290279
TI Synthesis and biological activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3
AU **Fujishima, Toshie**; Liu, Zhaopeng; Miura, Daishiro; Chokki, Manabu; Ishizuka, Seiichi; **Konno, Katsuhiro**; **Takayama, Hiroaki**
CS Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, 199-0195, Japan
SO Bioorganic & Medicinal Chemistry Letters (**1998**), 8(16), 2145-2148
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Synthesis and biol. evaluation of all eight possible A-ring diastereomers of 2-methyl-20-epi-1,25-dihydroxyvitamin D3 are described. Among the analogs synthesized, 2.alpha.-methyl-20-epi-1.alpha.,25-dihydroxyvitamin

D3 exhibited exceptionally high potency. The double modification of 2-Me substitution and 20-epimerization yielded analogs with unique activity profiles.

IT **214351-95-8P 214351-96-9P 214351-98-1P 214351-99-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. activity of 2-methyl-20-epi analogs of 1.alpha.,25-dihydroxyvitamin D3)

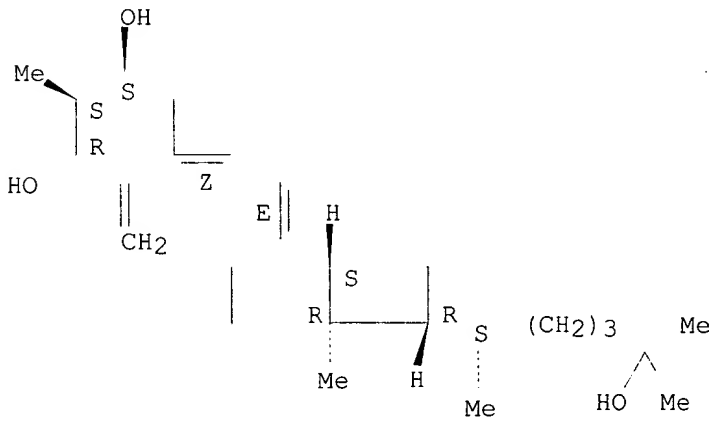
RN 214351-95-8 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 214351-96-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.alpha.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

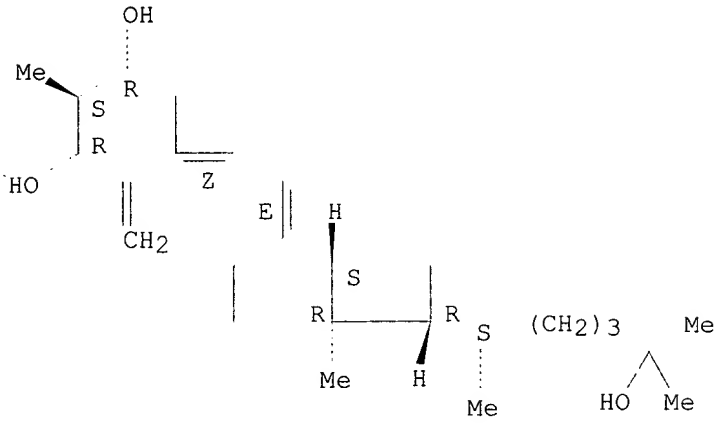
Absolute stereochemistry.
Double bond geometry as shown.



RN 214351-98-1 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.beta.,5Z,7E,20S)- (9CI) (CA INDEX NAME)

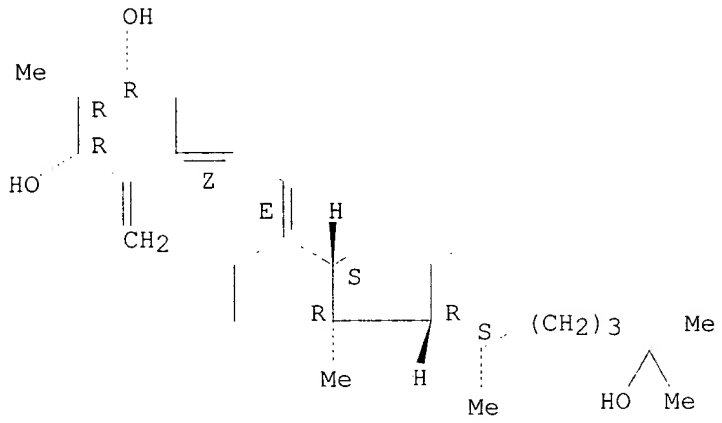
Absolute stereochemistry.

Double bond geometry as shown.

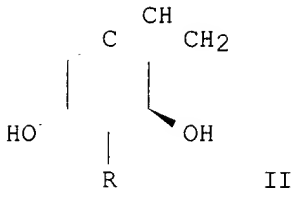


RN 214351-99-2 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.beta.,5Z,7E,20S)- (9CI) . (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L62 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:85846 HCAPLUS
DN 128:180577
TI A novel and practical route to A-ring enyne synthon for 1.alpha.,25-dihydroxyvitamin D3 analogs: synthesis of A-ring diastereomers of 1.alpha.,25-dihydroxyvitamin D3 and 2-methyl-1,25-dihydroxyvitamin D3
AU **Konno, Katsuhiro**; Maki, Shojiro; **Fujishima, Toshie**; Liu, Zhaopeng; Miura, Daishiro; Chokki, Manabu; **Takayama, Hiroaki**
CS Faculty Pharmaceutical Sciences, Teikyo Univ., Sagamiko, Kanagawa, 199-01, Japan
SO Bioorganic & Medicinal Chemistry Letters (**1998**), 8(2), 151-156
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 128:180577
GI



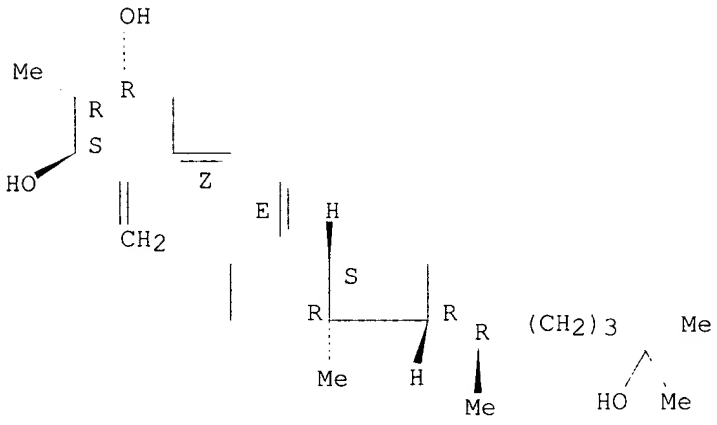
II

AB A novel and practical route to the A-ring enyne synthon II (R = H, Me), which can be versatile for a variety of A-ring analogs of 1.alpha.,25-dihydroxyvitamin D3 (I), was developed. This novel method led to an improved synthesis of the A-ring diastereomers of I, and synthesis of the new analogs, 2-methyl-1,25-dihydroxyvitamin D3 with its all possible diastereomers. The biol. evaluation of the 2-Me analogs showed the .alpha..alpha..beta.-isomer to be more potent than I.

IT **158388-11-5P 203126-73-2P 203126-91-4P 203126-92-5P 203126-93-6P 203126-94-7P 203126-95-8P 203126-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of A-ring enyne synthons and 1.alpha.,25-dihydroxyvitamin D3 analogs)

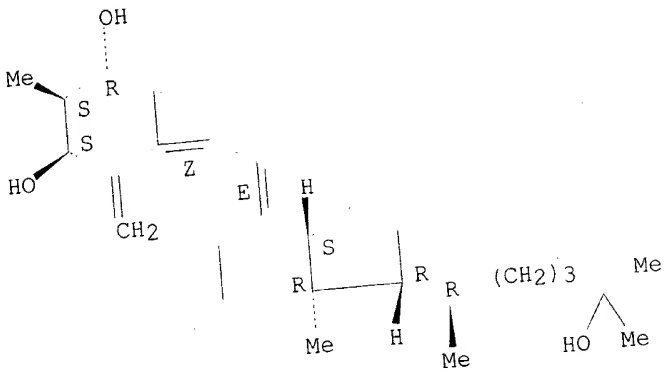
RN 158388-11-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



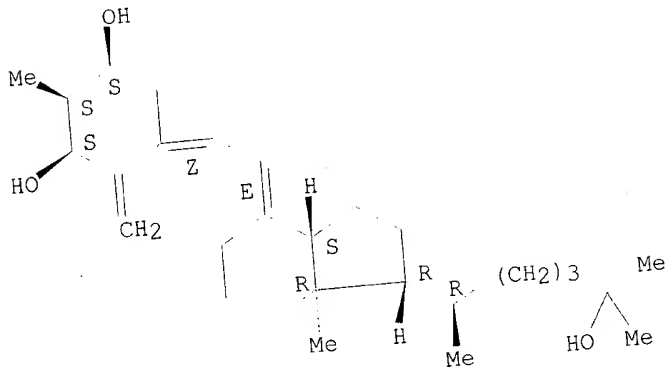
RN 203126-73-2 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



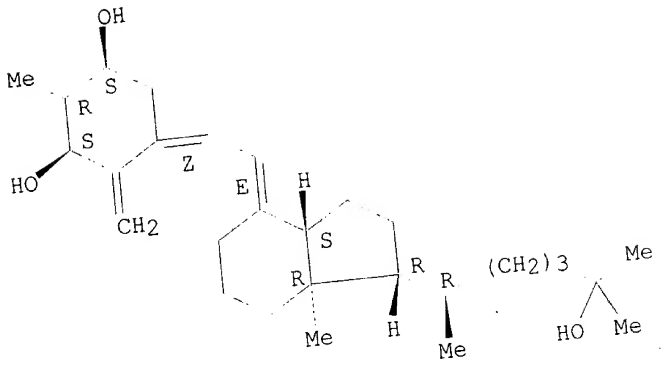
RN 203126-91-4 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.alpha.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



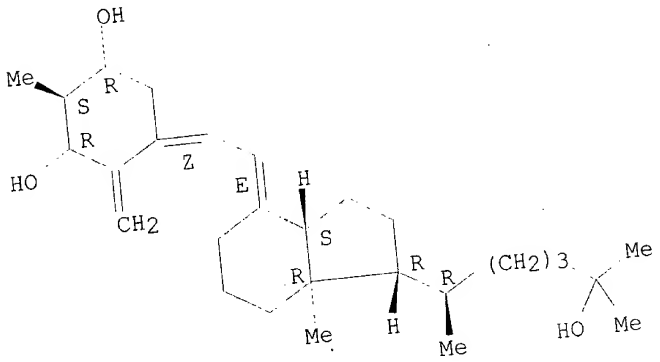
RN 203126-92-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



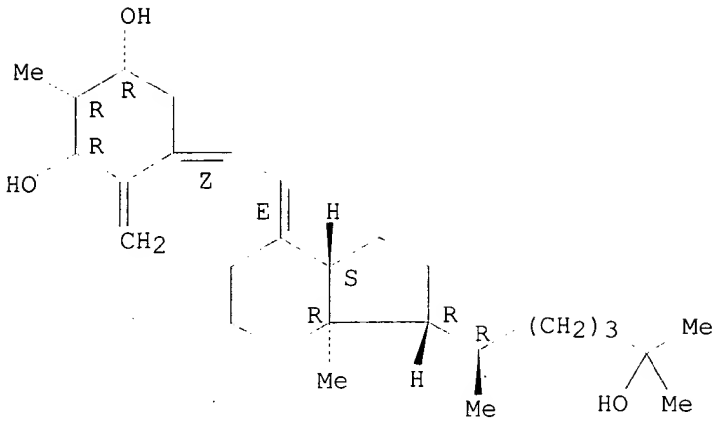
RN 203126-93-6 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



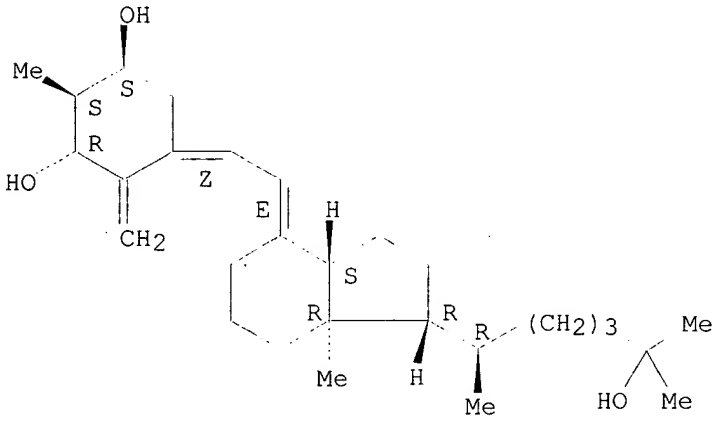
RN 203126-94-7 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



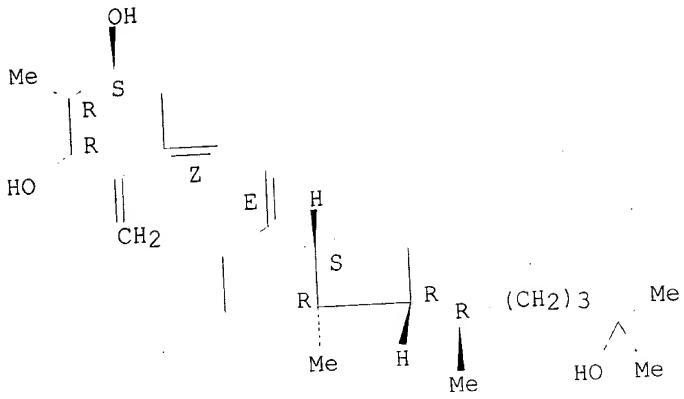
RN 203126-95-8 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.alpha.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 203126-96-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.beta.,2.beta.,3.alpha.,5Z,7E)- (9CI) (CA INDEX NAME)

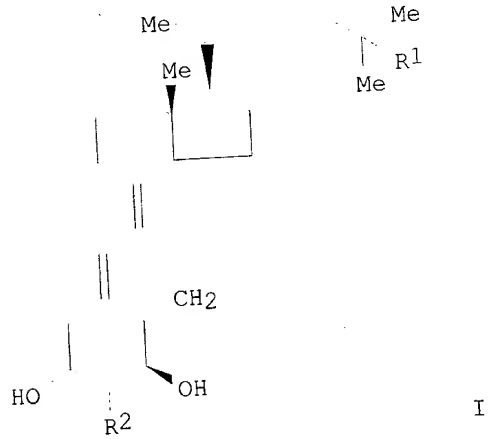
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L62 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:656121 HCAPLUS
DN 121:256121
TI 2.beta.-Substituted vitamin D derivatives
IN Myamoto, Katsuhito; Kubodera, Noboru
PA Chugai Pharmaceutical Co Ltd, Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06041059	A2	19940215	JP 1992-333441	19921030 <--
	JP 3213092	B2	20010925		
PRAI	JP 1991-349340	A1	19911101 <--		

OS MARPAT 121:256121
GI



I

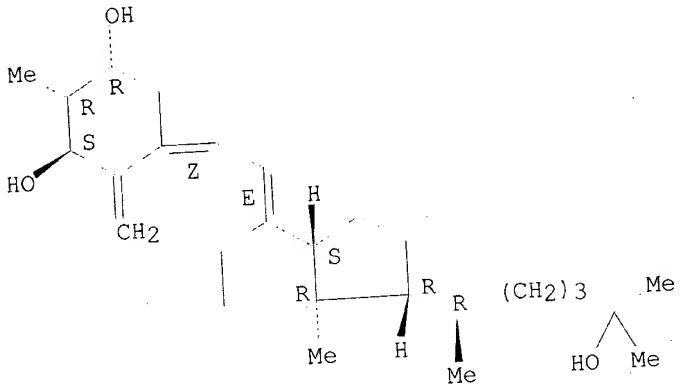
AB Title derivs. I (R1 = H, OH; R2 = lower alkyl, lower alkenyl, lower alkynyl; R2 may be substituted with OH, halogen, cyano, lower alkoxy, amino, or acylamino), useful for treatment of osteoporosis, are prepd. Thus, treating 1.alpha.,2.alpha.-epoxy-5.alpha.,8.alpha.-(3,5-dioxo-4-phenyl-1,2,4-triazoridino)-6-cholesten-3.beta.-ol with EtMgBr in THF under

Ar gave 69% 2.beta.-ethyl-1.alpha.,3.beta.-dihydroxy-5,7-cholestadiene, 32.6 mg of which was dissolved in EtOH and UV-irradiated to give 0.59 mg 2.beta.-ethyl-1.alpha.,3.beta.-dihydroxy-9,10-secocholesta-5,7,10(19)-triene.

IT **158388-11-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of osteoporosis)

RN 158388-11-5 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



=> fil uspatall
FILE 'USPATFULL' ENTERED AT 08:13:57 ON 30 MAY 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 08:13:57 ON 30 MAY 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot 163

L63 ANSWER 1 OF 2 USPATFULL
AN 2000:128309 USPATFULL
TI Vitamin D derivative with substituent at the 2.beta.-position
IN Miyamoto, Katsuhito, Tokyo, Japan
Kubodera, Noboru, Shizuoka-ken, Japan
PA Chugai Seiyaku Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)
PI US 6124276 20000926
AI US 1998-116999 19980717 (9)
RLI Division of Ser. No. US 1996-706969, filed on 3 Sep 1996, now patented, Pat. No. US 5877168 which is a continuation of Ser. No. US 1995-386544, filed on 10 Feb 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Badio, Barbara
LREP Browdy and Neimark
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1165
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 1.alpha.-hydroxy-vitamin D derivatives represented by formula ##STR1##

wherein R.sub.1 represents a hydrogen atom or a hydroxyl group; and R.sub.2 represents a straight-chain or branched C.sub.2 -C.sub.7 alkyl, C.sub.2 -C.sub.7 alkenyl, or C.sub.2 -C.sub.7 alkynyl group. The compounds exhibit calcium metabolism regulating activity and differentiation stimulating activity on tumor cells, and are useful as treating agents for diseases caused by abnormal calcium metabolism, such as osteoporosis and osteomalacia, or as antitumor agents.

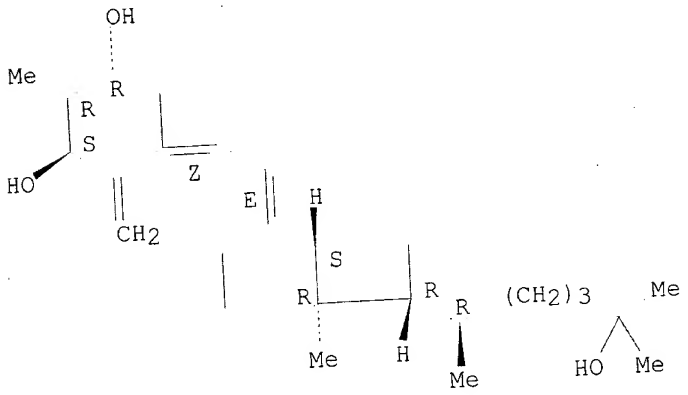
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **158388-11-5P**
(prepn. of 2.beta.-substituted vitamin D derivs. for the treatment of osteoporosis)

RN 158388-11-5 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L63 ANSWER 2 OF 2 USPATFULL

AN 1999:27627 USPATFULL

TI Vitamin D derivative with substituent at the 2.beta.-position

IN Miyamoto, Katsuhito, Tokyo, Japan
Kubodera, Noboru, Shizuoka-ken, Japan

PA Chugai Seiyaku Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)

PI US 5877168 19990302

AI US 1996-706969 19960903 (8)

RLI Continuation of Ser. No. US 1995-386544, filed on 10 Feb 1995, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Badio, Barbara

LREP Browdy And Neimark

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN 4 Drawing Figure(s); 4 Drawing Page(s)

LN.CNT 1234

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A 1.alpha.-hydroxy-vitamin D derivative represented by formula (I): ##STR1## wherein R.sub.1 represents a hydrogen atom or a hydroxyl group; and R.sub.2 represents a straight-chain or branched lower alkyl, lower alkenyl or lower alkynyl group, which is substituted with a hydroxyl group, a halogen atom, a cyano group, a lower alkoxy group, an amino group or an acylamino group,

is disclosed. The compound exhibits calcium metabolism regulating activity and differentiation stimulating activity on tumor cells, etc. and is useful as a treating agent for diseases caused by abnormal calcium metabolism, such as osteoporosis and osteomalacia, or as an antitumor agent.

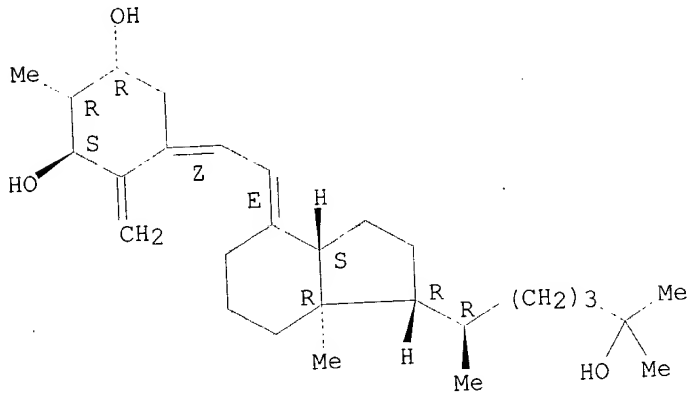
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **158388-11-5P**
(prepn. of 2.beta.-substituted vitamin D derivs. for the treatment of osteoporosis)

RN 158388-11-5 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 2-methyl-, (1.alpha.,2.beta.,3.beta.,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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FILE 'HCAPLUS' ENTERED AT 07:38:06 ON 30 MAY 2002
E TAKAYAMA H/AU
L1 258 S E3,E30
E KONNO K/AU
L2 196 S E3,E15,E7
E FUJISHIMA T/AU
L3 35 S E3,E29
E HIROAKI T/AU
L4 4 S E3
E KATSUHIRO K/AU
E TOSHIE F/AU
E TEIJIN/PA,CS
L5 18425 S E1-E4
L6 18841 S L1-L5
L7 331 S L6 AND ?VITAMIN?(L)D3#
L8 2 S L7 AND 20S
L9 54 S L7 AND 20
E WO98-JP1979/AP,KPRN
E WO98-JP1979/AP,PRN
L10 1 S E3,E4
E JP97-114695/AP,PRN
L11 2 S E4

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L12           2 S L10,L11 AND L6-L11
L13           4 S L8,L12
                SEL RN

      FILE 'REGISTRY' ENTERED AT 07:43:24 ON 30 MAY 2002
L14         127 S E1-E127
L15          43 S L14 AND 3/NR
L16          35 S L15 AND  C5-C6/ES AND C6/ES
L17          27 S L16 NOT SI/ELS
L18          19 S L17 AND C28H46O3
L19           8 S L18 NOT 20S
L20          11 S L18 NOT L19
L21           1 S L20 AND 1 BETA AND 2 BETA AND 3 ALPHA
L22           1 S L20 AND 1 ALPHA AND 2 ALPHA AND 3()(BETA OR ALPHA)
L23           1 S L20 AND 1 ALPHA AND 2 BETA AND 3 BETA
L24           2 S C28H46O3 AND C6/ES AND C5-C6/ES AND 20S AND 1 ALPHA AND 2 ALP
L25          33 S C28H46O3 AND C6/ES AND C5-C6/ES AND 20S
L26           2 S L25 AND 1 BETA AND 2 BETA AND 3 ALPHA
L27           2 S L25 AND 1 ALPHA AND 2 BETA AND 3 BETA
L28           2 S L25 AND 1 ALPHA AND 2 ALPHA AND 3 BETA
L29           2 S L25 AND 1 ALPHA AND 2 ALPHA AND 3 ALPHA
L30           8 S L21-L24,L26-L29
                SAV TEMP L30 QAZI214/A
                SEL RN
L31           0 S E128-E135/CRN

      FILE 'HCAOLD' ENTERED AT 07:57:48 ON 30 MAY 2002
L32           0 S L30

      FILE 'USPATFULL, USPAT2' ENTERED AT 07:57:53 ON 30 MAY 2002
L33           0 S L30

      FILE 'HCAPLUS' ENTERED AT 07:57:57 ON 30 MAY 2002
L34           8 S L30
L35           8 S L34 AND L6
L36           2 S L35 AND (PD<=19980430 OR PRD<=19980430 OR AD<=19980430)
L37           1 S L13 AND L36
L38           2 S L36,L37
L39           3 S L13 NOT L34
L40           2 S L39 AND (20S OR 20 (L) EPI?)
L41           3 S L39,L40

      FILE 'REGISTRY' ENTERED AT 08:01:41 ON 30 MAY 2002

      FILE 'HCAPLUS' ENTERED AT 08:01:51 ON 30 MAY 2002
L42           6 S L34 NOT L38
L43          13 S L9 AND EPI?
L44           7 S L8,L43 NOT L34-L38

      FILE 'REGISTRY' ENTERED AT 08:04:59 ON 30 MAY 2002
L45             STR
L46           3 S L45 CSS
L47          54 S L45 CSS FUL
                SAV TEMP L47 QAZI214155/A
L48          46 S L47 NOT L30

      FILE 'HCAOLD' ENTERED AT 08:08:21 ON 30 MAY 2002
L49           0 S L48

      FILE 'USPATFULL, USPAT2' ENTERED AT 08:08:27 ON 30 MAY 2002
L50           2 S L48

      FILE 'HCAPLUS' ENTERED AT 08:09:05 ON 30 MAY 2002
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L51          21 S L48
L52           8 S L51 AND (PD<=19980430 OR PRD<=19980430 OR AD<=19980430)
L53           4 S L52 AND L6
L54           8 S L52,L53
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:10:12 ON 30 MAY 2002
L55          19 S E136-E154
L56          18 S L48 NOT 2 METHYL
L57          28 S L48 NOT L56

     FILE 'HCAPLUS' ENTERED AT 08:12:35 ON 30 MAY 2002
L58          15 S L57
L59           6 S L58 AND (PD<=19980430 OR PRD<=19980430 OR AD<=19980430)
L60          12 S L58 AND L6
L61           4 S L59 AND L60
L62           6 S L59,L61

     FILE 'USPATFULL, USPAT2' ENTERED AT 08:13:24 ON 30 MAY 2002
L63           2 S L57

     FILE 'REGISTRY' ENTERED AT 08:13:33 ON 30 MAY 2002

     FILE 'HCAPLUS' ENTERED AT 08:13:46 ON 30 MAY 2002

     FILE 'USPATFULL, USPAT2' ENTERED AT 08:13:57 ON 30 MAY 2002

     FILE 'REGISTRY' ENTERED AT 08:14:52 ON 30 MAY 2002
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